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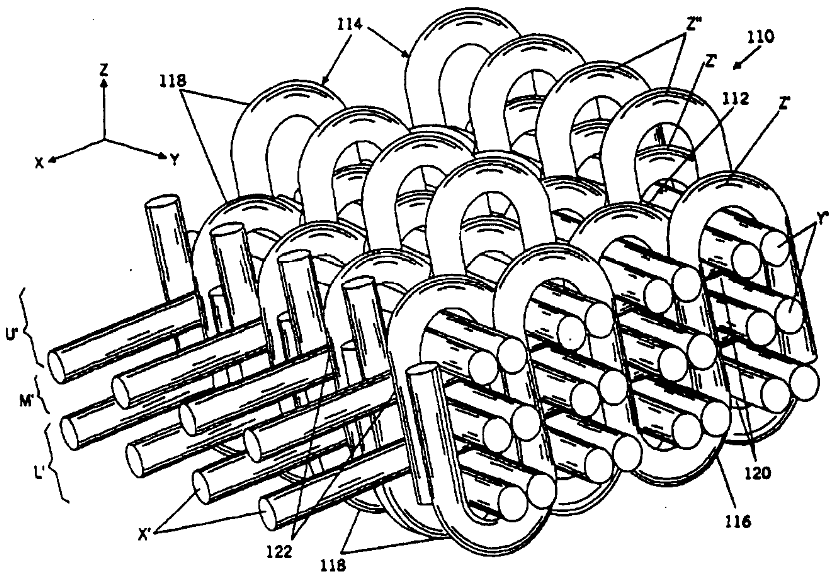
(54) Title: THREE-DIMENSIONAL FIBER SCAFFOLDS FOR INJURY REPAIR



(57) Abstract: A three-dimensional fiber scaffold (10) for injury repair, and methods of making and using the same. The scaffold includes at least three systems of fibers, wherein two of the three fiber systems define an upper layer (U), a lower layer (L) and a medial layer (M) between the upper layer and the lower layer within the three-dimensional fiber scaffold, wherein one of the three fiber systems interconnects the upper layer, and the medial layer, and wherein the three fiber systems are each made of a bio-compatible material.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Description

THREE-DIMENSIONAL FIBER SCAFFOLDS FOR INJURY REPAIR

Technical Field

The present invention relates to a three-dimensional fiber scaffold for injury repair. The scaffold is characterized by improved strength, porosity, flexibility and shrinkage resistance properties and is preferred for use in repair of hernias and similar injuries and traumas.

Background Art

Francis C. Usher first detailed the use of high density polyethylene in the repair of chest and abdominal wall defects in 1959. Since this time, numerous other synthetics have been used in the construction of mesh prostheses. The use of prosthetic mesh bio-compatible materials has allowed surgeons the ability to reconstruct hernia defects in a way that reduces the number of recurrent incidences as well as reducing post-operative pain and recovery time. However, there remains a significant need in the art for improved materials that can provide mechanical reinforcement to an injured abdominal or chest wall, especially wounds of very large size (e.g. ≥ 10 centimeters (cm) X 10 cm), while yielding minimal adverse biological response. The improved materials should exhibit a particular combination of strength, flexibility, and bio-compatibility characteristics.

For applications that require substantial tensile strength for an extended period of time (e.g., hernia repair), current efforts in the art employ non-absorbable materials. Polyester, polytetrafluoroethylene, and polypropylene are commonly found in commercially available products. However, currently available products tend to lack adequate tensile strength and can also include small pores, on the order of 10 micrometers (μm), that allow bacteria (approximately 1 μm) to establish a nidus in an area unaccessible to larger macrophage and neutrophilic granulocytes. Goldstein, H.S., *Hernia*, 3(1):pp23-26, February, 1999. The result is untreatable infection that warrants the removal of the prosthesis. Thus, the need to maintain the implant within a

subject for an extended period of time is not met.

Absorbable meshes have been formed from polyglycolic acid and polylactic acid fibers, but with marginal results. It has been reported in several studies that prostheses constructed from purely absorbable fibers hydrolyze and lose their strength before sufficient fibrous ingrowth occurs. Lamb, J.P. et al., *Surgery*, 93(5):pp 643-648, (May 1983); Tyrell, J. et al., *Surgery, Gynecology and Obstetrics*, 168(3):pp 227-32, (March 1989); and Rath, A.M. et al., *Chirurgie*, 121(4):pp 253-65, (1996).

Implantable meshes are generally formed through warp knit processes, yet woven fabrics and extruded films are also used. See Benchetrit, S. et al., *Hernia*, 2(2):pp 57-62, April, (1998). Warp knits generally employ filaments on the order of 5 to 15 thousandths of an inch in diameter (125 μm to 380 μm), as disclosed in U. S. Patent No. 5,634,931 to Kugel (assignee: Surgical Sense, Inc.), and in U. S. Patent No. 5,569,273 to Titone, M.A., and Herzog, D (assignee: C. R. Bard, Inc.).

Amid, P.K., *Hernia*, 1(1):pp 15-21, May 1997 characterized existing abdominal wall reconstruction prostheses in the art, and derived classifications based on material pore size as follows:

Type I: Totally macroporous prostheses (pore size > 75 μm)

These prostheses are usually open, low basis weight mesh fabrics formed by the knitting or weaving of monofilament fibers. Examples of macroporous prostheses are sold under the following registered trademarks: PROLENE® by Johnson & Johnson of New Brunswick, New Jersey, MARLEX® by C. R. Bard, Inc. of Murray Hill, New Jersey, and TRELEX NATURAL® by Meadox Medicals, Inc. of Oakland, New Jersey.

Type II: Totally microporous prostheses (pore size < 10 μm)

Biomaterials belonging to this class consist of pore sizes that are less than 10 μm. These are usually expanded polytetrafluoroethylene (ePTFE) sheets where irregular pores are formed by drawing the material during manufacturing processes. Prostheses in this class are poor at incorporating host tissue because their pores are generally too small to support cell ingrowth and proliferation. An example of a totally microporous prostheses is sold under

the registered trademark DUALMESH® by W. L. Gore & Associates, Inc. of Newark, Delaware.

Type III: Macroporous prostheses with microporous components (pore size > 75 μm & pore size < 10 μm).

These devices are similar to Type I prostheses; however, they are formed using braided components or yarns instead of monofilament. The result is a prosthesis that contains large pores within its macrostructure and small pores within its constituent yarns. As noted above, the small pores, on the order of 10 micrometers (μm), can allow bacteria (approximately 1 μm) to establish a nidus in an area unaccessible to larger macrophage and neutrophilic granulocytes. Perforated Type II prostheses, namely those sold under the registered trademark MYCROMESH® by W. L. Gore & Associates, Inc. of Newark, Delaware, can also be categorized in this class.

Type IV: Submicronic prostheses (pore size < 1 μm)

Containing pores of less than one micrometer, Type IV prostheses are unsuitable for use in abdominal wall reconstruction. However, they are sometimes used in conjunction with Type I prostheses in attempts to form an adhesion-free composite for intraperitoneal repairs.

An ideal prosthetic mesh or scaffold would display characteristics including but not limited to resistance to infection, pore characteristics that facilitate tissue incorporation, pliability, mechanical integrity and bio-compatibility. Such a mesh is not currently available in the art. Indeed, there is a continuing and long-felt need in the art for an improved injury patch scaffold material that possesses desired strength, resorbability, porosity, flexibility and shrinkage resistance characteristics.

Toward these ends, applicants have developed a new three-dimensional fiber scaffold for use in injury repair, including but not limited to hernia repair, wherein the three-dimensional fiber scaffold possesses improved strength, resorbability, porosity, flexibility and shrinkage resistance characteristics. Applicants believe that the three-dimensional fiber scaffold is new in the injury repair product art and meets a long-felt need for such a product; for a method for making the product; and for a method of treating an injury using the product.

Summary of the Invention

The present invention comprises a three-dimensional fiber scaffold for use in injury repair, the scaffold comprising at least three systems of fibers, wherein two of the three fiber systems define an upper layer, a lower layer and a medial layer between the upper layer and the lower layer within the three-dimensional fiber scaffold, wherein one of the at least three fiber systems interconnects the upper layer, the lower layer and the medial layer, wherein the at least three fiber systems each comprise a bio-compatible material. The bio-compatible material can comprise a material selected from the group including but not limited to an absorbable material, a non-absorbable material and combinations thereof.

Accordingly, it is an object of the present invention to provide a novel three-dimensional fiber scaffold for use in injury repair. The object is achieved in whole or in part by the present invention.

An object of the invention having been stated hereinabove, other objects will become evident as the description proceeds when taken in connection with the accompanying Drawings as best described herein below.

Brief Description of the Drawings

Figure 1 is a perspective view of a first embodiment of a three-dimensional orthogonally woven fiber scaffold product of the present invention;

Figure 2 is a top view of a first embodiment of a three-dimensional orthogonally woven fiber scaffold product of the present invention;

Figure 3 is a side view of a first embodiment of a three-dimensional orthogonally woven fiber scaffold product of the present invention;

Figure 4 is a schematic view of a process used in the manufacture of a three-dimensional fiber scaffold product of the present invention;

Figure 5 is a perspective view of an alternative embodiment of a three-dimensional orthogonally woven fiber scaffold product of the present invention; and

Figure 6 is a schematic view of a process used in the manufacture of the alternative embodiment of a three-dimensional orthogonally woven fiber scaffold product of the present invention depicted in Figure 5.

Detailed Description of the Invention

Applicants have developed a novel three-dimensional fiber scaffold that can be used in injury repair applications. The three-dimensional fiber scaffold comprises at least three systems of fibers, wherein two of the three fiber systems define an upper layer, a lower layer and a medial layer between the upper layer and the lower layer within the three-dimensional fiber scaffold, and wherein one of the at least three fiber systems interconnects the upper layer, the lower layer and the medial layer. The at least three fiber systems can each comprise a bio-compatible material, and the bio-compatible material preferably comprises an absorbable material, a non-absorbable material or combinations thereof.

Preferably, the three-dimensional fiber scaffold comprises a three-dimensional textile scaffold. In this case the fiber systems are referred to as yarn systems.

While the following terms are believed to be well understood by one of ordinary skill in the art, the following definitions are set forth to facilitate explanation of the invention.

The terms "injury" and "injury repair" are meant to refer any injury in a subject amenable to repair through implantation of a scaffold of the present invention; and preferably comprises an internal injury. Representative internal injuries can include but are not limited to abdominal trauma, visceral injuries, thoracoabdominal trauma, retroperitoneal organ injury, intraperitoneal injury, intra-abdominal bleeding due to blunt trauma, traumatic and non-traumatic perforation of hollow viscera, penetrating injury, abdominal gunshot injury, abdominal shrapnel, abdominal carcinoma, diaphragmatic rupture, stomal hernia, incisional hernia, inguinal hernia, and umbilical hernia. The term "injury" can thus include small wound and in a preferred embodiment refers to very large wounds (e.g. ≥ 10 cm X 10 cm). Other injuries that can be treated via

implantation of a scaffold of the present invention would be apparent to one of ordinary skill in the art after review of the disclosure herein.

The terms "bio-compatible" and "medically acceptable" are used synonymously herein and are meant to refer to a material that is compatible with a biological system, such as that of a subject having an injury to be repaired in accordance with the present invention. Thus, the term bio-compatible is meant to refer to a material that can be implanted internally in a subject as described herein.

The term "absorbable" is meant to refer to a material that tends to be absorbed by a biological system into which it is implanted. Representative absorbable fiber materials include but are not limited to polyglycolic acid (PGA), polylactic acid (PLA), polyglycolide-lactide, polycaprolactone, polydioxanone, polyoxalate, a polyanhydride, a poly(phosphoester), catgut suture, collagen, silk, chitin, chitosan, hydroxyapatite, bioabsorbable calcium phosphate, hyaluronic acid, or any other medically acceptable yet absorbable fiber. A preferred absorption or degradation time of absorbable fibers ranges from about 6 to about 8 weeks, in accordance with the increasing strength of new tissue ingrowth. Absorption times that correspond to a rate of new tissue ingrowth facilitate bio-compatibility since fast and intimate tissue ingrowth into the scaffold is important to the repair of the injury.

The term "non-absorbable" is meant to refer to a material that tends not to be absorbed by a biological system into which it is implanted. Representative non-absorbable fiber materials include but are not limited to polypropylene, polyester, polytetrafluoroethylene (PTFE) such as that sold under the registered trademark TEFLON® by E.I. DuPont de Nemours & Co., expanded PTFE (ePTFE), polyethylene, polyurethane, polyamide, nylon, polyetheretherketone (PEEK), polysulfone, a cellulosic, fiberglass, an acrylic, tantalum, polyvinyl alcohol, carbon, ceramic, a metal (e.g., titanium, stainless steel) or any other medically acceptable yet non-absorbable fiber.

The term "resin" is used its art-recognized sense and refers to any natural or synthetic resin have characteristics suitable for use in accordance

with the present invention. Representative "resins" thus comprise bio-compatible resins.

The term "composite material", as used herein, is meant to refer to any material comprising two or more components. One of the components of the material can optionally comprise a resin.

Following long-standing patent law tradition, the terms "a" and "an" are meant to refer to one or more as used herein, including the claims.

A. Three-Dimensional Fiber Scaffold

The present invention provides a unique scaffold fabricated from true 3D-fiber architecture (no fiber crimp and no need for lamination of multiple layers). The three-dimensional fiber scaffold of the present invention is characterized by improved strength, porosity, flexibility and shrinkage resistance properties and is preferred for use in repair of hernias and similar injuries and traumas.

The entire structure of the scaffold can comprise a non-absorbable fiber material, such as polypropylene, polyester, polytetrafluoroethylene (PTFE) such as that sold under the registered trademark TEFLON® by E.I. DuPont de Nemours & Co., expanded PTFE (ePTFE), polyethylene, polyurethane, polyamide, nylon, polyetheretherketone (PEEK), polysulfone, a cellulosic, fiberglass, an acrylic, tantalum, polyvinyl alcohol, carbon, ceramic, a metal (e.g., titanium, stainless steel) or any other medically acceptable yet non-absorbable fiber.

Alternatively, the entire structure of the scaffold comprises an absorbable fiber material, such as polyglycolic acid (PGA), polylactic acid (PLA), polyglycolide-lactide, polycaprolactone, polydioxanone, polyoxalate, a polyanhydride, a poly(phosphoester), catgut suture, collagen, silk, chitin, chitosan, hydroxyapatite, bioabsorbable calcium phosphate, hyaluronic acid, or any other medically acceptable yet absorbable fiber.

As yet another alternative, the entire structure can optionally comprise a commingling of non-absorbable and absorbable fiber materials as stated above.

Fibers can be monofilament, multifilament, or a combination thereof, and can be of any shape or cross-section, e.g. bracket-shaped (i.e. [ ), polygonal, square, I-beam, inverted T shaped, or other suitable shape or cross-section. The cross-section can vary along the length of fiber. Fibers can also be hollow to serve as a carrier for chemicals (e.g., antibiotics, growth factors, etc.) as described herein. Setting of the yarn systems can be done via any of a number of art-recognized techniques, including but not limited to ultrasonication, a resin, infrared irradiation, heat or any combination thereof. Setting of the yarn systems within the scaffold in this manner provides cuttability and suturability. Sterilization is done by routine methods such as autoclave, radiation, hydrogen peroxide, ethylene oxide, and the like.

In a preferred embodiment, the scaffold of the present invention comprises a structure having loops formed by a z-yarn on the upper layer, and the upper layer comprises primarily absorbable fiber material (e.g., PGA), the medial layer comprises a mixture of absorbable and non-absorbable fibers (e.g., PGA and polypropylene), and the lower layer comprises primarily non-absorbable fibers (e.g., polypropylene). As disclosed herein, loop formation in z-yarns can be achieved by: (a) removal of fibers from the upper layer after the structure is woven; or (b) fabricating the scaffold with "dissolvable" fibers which can be removed by immersing the scaffold in a suitable solvent. A preferred thickness is of a 2-warp/3-fill configuration. Thicker scaffolds are preferred in very large wounds.

Each layer can optionally comprise pores or interstices. The sizes of the pores or the interstices can range from about 10 to about 250 μm, can more preferably range from about 25 to about 175 μm, and the most preferred pore size of ranges from about 50 to about 125 μm for optimal tissue incorporation. In a preferred embodiment of the scaffold of the present invention, going from the upper layer to the lower layer, the size of the pores within each layer is in descending order to facilitate cell contact guidance. A preferred pore size of the loops and of the pores in the upper layer ranges from about 50 to about 125 μm. The medial layer comprises pores that are smaller than the pores present in the upper layer. The lower layer comprises pores that are smaller

than the pores present in the medial layer, and the outer surface of the bottom layer has no pores. This can be achieved by selective heat treatment or melting of non-absorbable material (e.g. thermoplastic polypropylene) comprising the lower layer; by lamination or coating the bottom layer with a flat sheet of an non-absorbable material (e,g, polypropylene or PTFE) or of another suitable material (e.g., a hydrogel); and/or by impregnating or coating the bottom layer with a resin and then curing the resin. The lack of pores in the outer surface of the bottom layer substantially prevents adhesion to the peritoneal cavity.

The term "thermoplastic", as used herein, is meant to refer to materials, including yarns, fibers, threads, and the like, which are susceptible to becoming or remaining soft and moldable when subjected to heat. Preferred examples of suitable thermoplastic materials for use in accordance with the present invention include nylon, low-melt polyester and plastics. Preferred plastics include polyolefin fibers, polypropylene fibers, polyethylene fibers (such as those sold under the registered trademark SPECTRA® by Allied-Signal, Inc. of Morristown, New Jersey, those sold under the registered trademark DYNEEMA® by DSM High Performance Fibers B.V., Heerlen, Netherlands, or those that sold under the registered trademark CERTRAN® by Hoechst Celanese Corporation, Somerville, New Jersey), or copolymer combinations of any of the foregoing polymer fibers. Representative thermoplastic fibers are also disclosed in U.S. Patent Nos. 5,034,449; 5,219,628; 5,229,177; and 5,499,441, the entire contents of each of which herein incorporated by reference. Indeed, any suitable thermoplastic material as would be apparent to one of ordinary skill in the art after review of the disclosure presented herein is provided in accordance with the present invention.

Controlled cellular (preferably microcellular) matrix formation can optionally be employed in the bottom layer. The inclusion of a thermoplastic fiber in the bottom layer facilitates controlled microcellular matrix formation. Controlled microcellular matrix formation increases the strength properties of the scaffold material per unit weight by intentionally creating defined air voids throughout the bottom layer.

The entire scaffold can be impregnated with a therapeutic agent. Alternatively, a layer of the scaffold, or an individual fiber or fibers within the scaffold, can be coated or impregnated with a therapeutic agent. Where the scaffold comprises hollow fibers, a therapeutic agent can be loaded within the internal void space of the hollow fibers. The term "therapeutic agent" is meant to refer to any agent having a therapeutic effect at the site of the wound or injury where the scaffold is implanted.

Representative therapeutic agents include antibiotic (e.g. tetracycline, erythromycin, and the like), antimicrobial, anti-infective, and/or antibacterial materials. These materials are employed to reduce or eliminate any chance of infection, a consideration of importance for any injury, but of relatively more importance in large traumatic wounds. Examples of such materials include povidone/iodine, silver, silver oxide, other silver salt, copper salts, sulfadiazine, chlorhexidine, triclosan, cetyl ammonium chloride, cetyl ammonium bromide, quaternary amines and alkyl sulfonates.

Representative therapeutic agents also include but are not limited to cell growth modulating materials, such as purified type I collagen and gelatin. The materials are employed to further enhance tissue incorporation. Additional cell growth modulating materials include but are not limited to growth factors, cytokines, chemokines, or other chemicals that improve or enhance cellular infiltration, angiogenesis, and tissue regeneration, or to inhibit these properties as needed for specific applications. Particular cell growth modulating molecules, or fragments of molecules, include but are not limited to a collagen, gelatin, laminin, fibronectin, thrombin, lipids, cartilage oligomeric protein (COMP), thrombospondin, fibrin, fibrinogen, Matrix-GLA (glycine-leucine-alanine) protein, chondrocalcin, tenascin, a mineral, an RGD (Arginine-Glycine-Aspartic Acid) peptide or RGD-peptide containing molecule, elastin, hyaluronic acid, a glycosaminoglycan, a proteoglycan, water, or an electrolyte solution. Thus, the term "cell growth modulating material" refers to a material that can promote or inhibit cell or tissue growth.

Currently available prior art prosthetic injury repair products lack sufficient strength, particularly in large traumatic wounds. With larger defects,

surgeons frequently use silicone sheeting as a temporary device. Removal is necessary once the required tissues are formed. In marked contrast, the scaffolds of the present invention offer improved tissue incorporation, shrinkage resistance, flexibility and resorbability characteristics along with improved strength per unit weight characteristics along as compared to prior art prostheses constructed via different methods, resulting in outstanding load bearing capacity in the scaffold of the present invention, among other advantages. Larger defects can thus be repaired without using a temporary device.

B. Method of Making Three-Dimensional Fiber Scaffold

Referring now to Figures 1-6, applicants wish to describe a first and a second embodiment of a three-dimensional fiber scaffold of the present invention, as well as methods of making the same. While Figures 1-6 illustrate orthogonally woven three-dimensional fiber scaffolds, the invention is not intended to be limited to this structure but to include other three-dimensional fiber scaffolds formed of at least three systems of fibers so as to preferably provide interstices within the structure. These structures can include woven, braided, circular woven and knitted three-dimensional structures formed of at least three different fiber systems.

Well recognized methods for making three-dimensional structures comprising at least three fiber systems are generally applicable to the process of making a scaffold of the present invention. For example, the 3-D fabric can be fabricated on one of the 3-D weaving machines located at 3TEX, Inc., Cary, North Carolina. Representative methods of making three-dimensional textile structures are also disclosed in U.S. Patent No. 5,465,760 issued to Mohamed et al. on November 14, 1995 and U.S. Patent No. 5,085,252 issued to Mohamed et al. on February 4, 1992, and the contents of each of these U.S. patents are herein incorporated by reference.

1. First Embodiment

Referring now to Figures 1-3, a volumetric section of a first embodiment of a three-dimensional woven scaffold according to the present invention is shown and generally designated **10**. Three-dimensional textile scaffold **10** preferably comprises at least three primary systems of fibers. A first system includes a plurality of x-fibers (or warp fibers) **X** running straight and in a spaced parallel relation along the x-axis. A second system includes a plurality of y-fibers (or fill or weft fibers) **Y** running straight and in a spaced parallel relation along the y-axis. In scaffold **10**, y-fibers **Y** are actually one or more single, continuous fibers that are extended in one direction along the y-axis across the plane defined by the first system of x-fibers, and then made to reverse direction in a repeated manner around loops or curved sections **12** at the fold of scaffold **10** so as to extend across the plane of the first system in the opposite direction. It is preferable that x-fibers **X** and y-fibers **Y**, and thus the first and second systems, be disposed in a mutually orthogonal relation, such that the x- and y-axes are defined as in a Cartesian coordinate system.

Continuing with Figures 1-3, a third system includes a plurality of z-fibers **Z** running in parallel relation through the planes of x-fibers **X** and y-fibers **Y**, such that z-fibers **Z** can be said to interconnect or bind the first and second systems and, in the case of a multiple-layered scaffold, to interconnect or bind all layers forming scaffold **10**. Preferably, z-fibers **Z** generally extend along the Cartesian z-axis such that z-fibers **Z** are mutually orthogonal to both x-fibers **X** and y-fibers **Y** or, stated differently, the third system is preferably disposed in an out-plane that is perpendicular to the in-plane defined by the first and second systems. Alternatively, or in addition to the orthogonal z-fibers **Z**, scaffold **10** can include fibers running along a bias direction, or a direction angled with respect to the Cartesian axes. It is further preferable that z-fibers **Z** comprise one or more fibers which extend through the first and second systems in one direction along the z-axis and reverse direction in a repeated manner around curved sections **14** at the edge of scaffold **10**.

Continuing with Figures 1-3, fiber systems **X** and **Y** define an upper layer **U**, a lower layer **L**, and a medial layer **M** between upper layer **U** and lower layer

L, within the three-dimensional scaffold **10**. The terms "upper layer", "medial layer", and "lower layer" have been adopted to facilitate description of scaffold **10**, and upon implantation, lower layer **L** comprises the peritoneal side of scaffold **10**. Each layer can be defined as including one system of x-fibers **X** and one system of y-fibers **Y**, except for the outermost surface layers where only y-fibers **Y** are present. The actual number of layers, and the number of individual fiber systems included within each layer, will depend upon the desired thickness of the finished scaffold. Fiber system **Z** interconnects upper layer **U**, lower layer **L** and medial layer **M**.

Continuing with Figures 1-3, fiber systems **X**, **Y** and **Z** are preferably interlaced so as to provide a plurality of pores or interstices **16** within textile scaffold **10**. Indeed, it is preferred that the inventive scaffold **10** is not crimped so that interstices **16** remain intact after the intermeshing of fiber systems **X**, **Y** and **Z**. More preferably, fiber systems **X**, **Y** and **Z** are secured to each other at one or more contact points **18** to facilitate maintenance of interstices **16** while also providing cuttability and suturability. The securing or setting of fiber systems **X**, **Y** and/or **Z** at a contact point **18** can be accomplished by any suitable technique, such as sonication or heat molding. The sizes of the pores or interstices can range from about 10 μm to about 250 μm, can more preferably range from about 25 μm to about 175 μm, and the most preferred pore size of ranges from about 50 μm to about 125 μm for optimal tissue incorporation. In scaffold **10**, interstices **16** are of a substantially uniform size throughout each of upper layer **U**, medial layer **M** and lower layer **L**.

As best seen in Figure 3, an outer surface **20** of lower layer **L** of textile scaffold **10** has no pores or interstices. This can be accomplished by coating outer surface **20** with a resin material **R**, preferably to the extent that resin material **R** coats all of outer surface **20**. Alternatively, outer surface **20** can be covered with an inert material, e.g. polytetrafluoroethylene (PTFE) such as that sold under the registered trademark TEFLON® by E.I. DuPont de Nemours & Co. For example, outer surface **20** can be covered with a sheet of PTFE. As an additional alternative, outer surface **20** can be tightly woven with

substantially no pores. Thus, outer surface **20** can optionally comprise a sealed surface or a smooth sealed surface.

Properties of scaffold **10** can further be enhanced with controlled cellular matrix formation within resin material **R** as disclosed in pending U.S. Patent Application Serial No. 09/376,109, herein also incorporated by reference. Briefly, a foamable polymer resin material **R** is applied to a portion of three-dimensional textile scaffold **10** (preferably lower layer **L**) so as to fill interstices **16** and impregnate a portion of the three-dimensional textile scaffold **10**. Then, foamable polymer material **R** is foamed to produce a cellular foamed polymer matrix material **R** containing a plurality of voids or cells distributed substantially throughout the material **R**. Preferably, the cellular matrix within material **R** comprises bubbles defining a void diameter of between about 0.01 µm to 10.0 µm, but cell void diameter can be larger. The cellular matrix increases the strength and stiffness properties of the material per unit weight by intentionally creating defined air voids throughout the composite structure.

As an alternative to the application of resin material **R**, a portion of scaffold **10** of the present invention can be heat-molded if the portion of scaffold **10** comprises thermoplastic fibers. As part of this process the thermoplastic portion can be foamed directly to provide a cellular matrix therein.

Representative foaming techniques are also disclosed in U.S. Patent No. 3,796,779 issued to Greenberg; U.S. Patent No. 4,473,665 to J.E. Martini-Vredrensky et al.; U.S. Patent No. 4,761,256 to Hardenbrook et al.; and U.S. Patent No. 5,334,356 and U.S. Patent No. 5,158,986 both issued to Baldwin et al. The entire contents of each of these U.S. Patents are herein incorporated by reference.

The process by which scaffold **10** is formed will now be further described with reference to the schematic shown in Figure 4. Lengthwise or x-fibers **X** are drawn under tension from an x-fiber feeding device **32** such as a set of warp beams (as shown) or a creel (not shown), between heddles **34** of harnesses **36**, and through a beat-up reed **38**, thereby forming systems of x-fibers **X** which are in horizontal and vertical alignment. Crosswise or y-fibers **Y** (not shown) are inserted between the systems of x-fibers **X** using fill insertion

rapiers **42**. Preferably, all y-fibers **Y** are inserted simultaneously in order to guarantee their straightness within the core of finished scaffold **10** and to increase productivity. Beat-up reed **38** is actuated to apply force on y-fibers **Y** as scaffold **10** is being formed, thereby packing x-fibers **X** and y-fibers **Y** into a structure having interstices or pores of a desired pore size. It will be understood that other devices, such as a conventional selvedge hold device **44** (for preventing the selvedge or edge on either side of the fabric from unraveling) and fill hold device **46** (for tensioning of y-fibers **Y**), are preferably employed in known manner during the forming of scaffold **10**.

Z-fibers **Z** are drawn under tension from a z-fiber feeding device **48** such a creel with bobbins (as shown) or one or more beams (not shown), and inserted through the layers formed by the systems of x-fibers **X** and y-fibers **Y** under the control of harnesses **36** with cross-moving heddles **34** and beat-up reed **38**. Take-up roll **52** is used to advance scaffold **10** forwardly. One specific and exemplary process and apparatus that can be utilized to form a structure such as scaffold **10** is described in detail in U.S. Patent No. 5,085,252 to Mohamed et al., which applicants incorporate herein by reference.

The thickness and composition of the layers of scaffold **10**, and thereby of the entire structure, can be altered and customized to fit a variety of injury and trauma repair applications. A preferred thickness is of a 2-warp/3-fill configuration. Thicker scaffolds are preferred for very large wounds. Additional fiber systems **X** and **Y** can be included within any of upper layer **U**, lower layer **L** and medial layer **M** of textile scaffold **10**. For example, (+)/(-) bias fibers can be incorporated within textile scaffold **10** in accordance with techniques described in U.S. Patent No. 5,465,760. Thus, textile scaffold **10** having more than three fiber systems are also provided in accordance with the present invention, including textile scaffolds having four and five fiber systems. The additional fiber systems can comprise absorbable materials, non-absorbable materials, or combinations thereof, depending on the particular application for the scaffold.

In a preferred embodiment of the scaffold **10** of the present invention, the fiber systems **X** and **Y** which define upper layer **U** comprise primarily an

absorbable material as defined herein; the fiber systems **X** and **Y** which define lower layer **L** comprise primarily a non-absorbable material as defined herein; and the fiber systems **X** and **Y** which define medial layer **M** comprise both absorbable and non-absorbable materials as defined herein. Fiber systems **X** and **Y** which define upper layer **U** can also comprise a relatively smaller proportion of non-absorbable material. Correspondingly, fiber systems **X** and **Y** which define lower layer **L** can also comprise a relatively smaller proportion of an absorbable material. This construction can be accomplished by incorporating more filaments of an absorbable material as compared to non-absorbable material into the fiber systems **X** and **Y** which comprise upper layer **U**; and incorporating relatively more non-absorbable filaments as compared to absorbable filaments into fiber systems **X** and **Y** which define lower layer **L**, as a part of a weaving, knitting, braiding or other process for interlacing fiber systems **X** and **Y** to form textile scaffold **10**. The filaments can be either twisted, zero-twisted, or both. Multifilament fibers are preferred for flexibility.

Thus, fiber systems **X** and **Y** can comprise both an absorbable material and a non-absorbable material in accordance with the present invention, as can fiber system **Z**. In the fiber systems **X** and **Y** that comprise upper layer **U**, and in fiber system **Z**, representative proportions of absorbable material to non-absorbable material can comprise 100/0, 90/10, 80/20, 70/30, 60/40, 50/50, 40/60, 30/70, 20/80, 10/90 or 0/100. In the first embodiment, representative proportions of absorbable material to non-absorbable material preferably comprise 100/0, 90/10, 80/20, 70/30 and 60/40. In the fiber systems **X** and **Y** that comprise lower layer **L**, and in fiber system **Z**, representative proportions of non-absorbable material to absorbable material can comprise 100/0, 90/10, 80/20, 70/30, 60/40, 50/50, 40/60, 30/70, 20/80, 10/90 or 0/100. In the first embodiment, representative proportions of non-absorbable material to absorbable material preferably comprise 100/0, 90/10, 80/20, 70/30 and 60/40. Medial layer **M** can comprise the noted proportions of either of upper layer **U** or lower layer **L**, or can comprise 50/50 absorbable/non-absorbable material. While representative proportions are provided herein, any suitable proportions can be employed in accordance with the present invention, and preferably,

proportions are chosen depending on a particular end use for the scaffold of the present invention.

2. Second Embodiment

Referring now to Figure 5 of the drawings, a volumetric section of a second embodiment of the three-dimensional woven scaffold according to the present invention is shown and generally designated **110**. Three-dimensional textile scaffold **110** preferably comprises at least three primary systems of fibers. A first system includes a plurality of x-fibers (or warp fibers) **X'** running straight and in a spaced parallel relation along the x-axis. A second system includes a plurality of y-fibers (or fill or weft fibers) **Y'** running straight and in a spaced parallel relation along the y-axis. In scaffold **110**, y-fibers **Y'** are laid in as pairs of fibers that extend along the y-axis across the plane defined by a system of x-fibers of scaffold **110**. Thus, scaffold **110**, and the method of making the same, provide preferred porosity characteristics as will be described herein below. It is also preferable that x-fibers **X'** and y-fibers **Y'**, and thus the first and second systems, be disposed in a mutually orthogonal relation, such that the x- and y-axes are defined as in a Cartesian coordinate system.

Continuing with Figure 5, a third system includes two sets of z-fibers **Z'** and **Z"** running in alternating parallel relation through the planes of x-fibers **X'** and y-fibers **Y'**. The z-fibers **Z'** can be said to interconnect or bind the first and second systems and, in the case of a multiple-layered scaffold, to interconnect or bind all layers forming scaffold **110**. The z-fibers **Z"** define loops **114** extending from upper surface **112** of three-dimensional fiber scaffold **110**. A preferred pore size of loops **114** ranges from about 50 to about 125 μm. Preferably, z-fibers **Z'** and **Z"** generally extend along the Cartesian z-axis such that z-fibers **Z'** and **Z"** are mutually orthogonal to both x-fibers **X'** and y-fibers **Y'** or, stated differently, the third system is preferably disposed in an out-plane that is perpendicular to the in-plane defined by the first and second systems. Alternatively, or in addition to the orthogonal z-fibers **Z'** and **Z"**, scaffold **110** can include fibers running along a bias direction, or a direction angled with

respect to the Cartesian axes. It is further preferable that z-fibers **Z'** and **Z"** comprise one or more fibers which extend through the first and second systems in one direction along the z-axis and reverse direction in a repeated manner around curved sections **118** at the upper surface **112** and the lower surface **116** of scaffold **110**.

Continuing with Figure 5, fiber systems **X'** and **Y'** define an upper layer **U'**, a lower layer **L'**, and a medial layer **M'** between upper layer **U'** and lower layer **L'**, within the three-dimensional structural scaffold **110**. The terms "upper layer", "medial layer", and "lower layer" have been adopted for convenience to facilitate description of scaffold **110**. Upon implantation, lower layer **L'** comprises the peritoneal side of scaffold **110**. Upper layer **U'** and lower layer **L'** each comprise one system of x-fibers **X'** and one system of y-fibers **Y'**, while medial layer **M'** comprise a system of y-fibers **Y'** only. The actual number of layers, and the number of individual fiber systems included within each layer, will depend upon the desired thickness of the finished scaffold. Fiber system **Z'** interconnects upper layer **U'**, lower layer **L'** and medial layer **M'**.

Continuing with Figure 5, fiber systems **X'**, **Y'**, **Z'** and **Z"** are preferably interlaced so as to provide a plurality of pores or interstices **120** within textile scaffold **110**. Indeed, it is preferred that the inventive scaffold **110** is not crimped so that interstices **120** remain intact after the intermeshing of fiber systems **X'**, **Y'**, **Z'** and **Z"**. More preferably, fiber systems **X'**, **Y'**, **Z'** and/or **Z"** are secured to each other at one or more contact points **122** to facilitate maintenance of interstices **120** while also providing cuttability and suturability. The securing or setting of fiber systems **X'**, **Y'**, **Z'** and/or **Z"** can be accomplished by any suitable technique, such as sonication or heat molding, at a contact point **122**. The sizes of interstices **120** can range from about 10 μm to about 250 μm, can more preferably range from about 25 μm to about 175 μm, and the most preferred pore size of ranges from about 50 μm to about 125 μm for optimal tissue incorporation. In scaffold **110**, the interstices **120** in upp r layer **U'** are larger that those present in medial layer **M'**, and the interstices **120** in medial layer **M'** are larger that those present in lower layer **L'**.

Thus, the size of the interstices **120** within each layer is in descending order from upper layer **U'** to lower layer **L'** to facilitate cell contact guidance.

The process by which scaffold **110** is formed will now be further described with reference to the schematic shown in Figure 6. The process by which scaffold **110** is formed is very similar to that depicted in Figure 4 and described above, except that a first set of harnesses **136** is used to introduce fiber systems **Z'** and a second set of harnesses **138** is used to introduce fiber systems **Z"**. The lift of the first set of harnesses **136** is mechanically limited so that the z-fibers **Z'** they carry cannot move above the plane of a third warp layer X'_3. These "short" z-fibers **Z'** bind the first and second warp layers X'_1 and X'_2 together with the first, second, and third weft layers Y'_1, Y'_2 and Y'_3. Z-fibers **Z"** are introduced into scaffold **110** via a second set of harnesses **138**. The lift of the second set of harnesses **138** is not mechanically limited in the manner of the first set of harnesses **136** and thus, the z-fibers **Z"** they carry move above the plane of a third warp layer X'_3 and a fourth weft layer Y'_4. Once woven, the fourth weft layer Y'_4 and subsequently, the third warp layer X'_3 are removed. Depending on the type of fiber used, removal can be accomplished by physically pulling out the fourth weft layer Y'_4 and the third warp layer X'_3 or by dissolving the fourth weft layer Y'_4 in a suitable medium and the third warp layer X'_3, if a degradable or soluble fiber was used. The "tall" z-fibers **Z"** introduced via the second set of harnesses **138** remain in place, now extending above an upper surface **112** of scaffold **110** to define a loop **114** (shown in Figure 5).

Thus, a preferred method of forming loop **114** on upper layer **U'** of scaffold **110** is using a modified pile weaving process. The formation of raised loops **114** on a 3-D orthogonally woven fabric requires the incorporation of an additional set of z-fibers **Z"**. Weaving proceeds in the conventional manner for a given number of insertions as the primary sets of z-fibers **Z'** interlace with the warp fibers (e.g. $X'_1, X'_2, X'_3, \ldots X'_N$) and weft fibers (e.g. $Y'_1, Y'_2, Y'_3, \ldots Y'_N$) to form the fabric; however, z-yarns **Z'** are not fully advanced into the fell of scaffold **110**. While these insertions take place, the additional z-yarns **Z"** remain stationary and are interlaced into scaffold **110** only upon completion of

the weft insertions (e.g. Y'_1, Y'_2, Y'_3, ... Y'_N). This action causes the added z-yarns **Z"** to form what is called a float. Once the float is formed, weft insertions (e.g. Y'_1, Y'_2, Y'_3, ... Y'_N) are fully advanced (beat-up) into the fell of scaffold **110**, causing the float to buckle and form loops **114** on the surface of scaffold **110**. As shown in Figure 6, these floats are formed by the introduction of additional z-yarns **Z"** through harnesses **136** whose lift is mechanically limited, as described immediately above.

The thickness and composition of the layers of scaffold **110**, and thereby of the entire structure, can be altered and customized to fit a variety of injury and trauma repair applications. It is preferred that a scaffold of the present invention be as thin as possible and yet maintain desired strength properties. A representative thickness is of a 2-warp/3-fill configuration. Thicker scaffolds are preferred for very large wounds. Additional fiber systems **X'** and **Y'** can be included within any of upper layer **U'**, lower layer **L'** and medial layer **M'** of textile scaffold **110**. For example, (+)/(-) bias fibers can be included within textile scaffold **110** in accordance with techniques described in U.S. Patent No. 5,465,760, herein incorporated by reference. Thus, textile scaffold **110** having more than three fiber systems are also provided in accordance with the present invention, including textile scaffolds having four and five fiber systems. The additional fiber systems can comprise absorbable materials, non-absorbable materials, or combinations thereof, depending on the particular application for the scaffold.

In a preferred embodiment of the scaffold **110** of the present invention, the fiber systems **X'** and **Y'** that define upper layer **U'** comprise primarily an absorbable material as defined herein; the fiber systems **X'** and **Y'** which define lower layer **L'** comprise primarily a non-absorbable material as defined herein; and the fiber system **Y'** which define medial layer **M'** comprises both absorbable and non-absorbable materials as defined herein. Fiber systems **X'** and **Y'** that define upper layer **U'** can also comprise a relatively smaller proportion of non-absorbable material. Correspondingly, fiber systems **X'** and **Y'** which define lower layer **L'** can also comprise a relatively smaller proportion of an absorbable material. This construction can be accomplished by

incorporating more filaments of an absorbable material as compared to non-absorbable material into the fiber systems **X'** and **Y'** which comprise upper layer **U'**; and incorporating relatively more non-absorbable filaments as compared to absorbable filaments into fiber systems **X'** and **Y'** which define lower layer **L'**, as a part of a weaving, knitting, braiding or other process for interlacing fiber systems **X'** and **Y'** to form textile scaffold **110**. The filaments can be either twisted, zero-twisted, or both. Multifilament fibers are preferred for flexibility.

Fiber systems **X'** and **Y'** can comprise both an absorbable material and a non-absorbable material in accordance with the present invention, as can fiber systems **Z'** and **Z"**. In the fiber systems **X'** and **Y'** that comprise upper layer **U**, and in fiber systems **Z'** and **Z"**, representative proportions of absorbable material to non-absorbable material can comprise 100/0, 90/10, 80/20, 70/30, 60/40, 50/50, 40/60, 30/70, 20/80, 10/90 or 0/100. In the second embodiment, representative proportions of absorbable material to non-absorbable material preferably comprise 100/0, 90/10, 80/20, 70/30 and 60/40. In the fiber systems **X'** and **Y'**, that comprise lower layer **L'**, and in fiber systems **Z'** and **Z"**, representative proportions of non-absorbable material to absorbable material can comprise 100/0, 90/10, 80/20, 70/30, 60/40, 50/50, 40/60, 30/70, 20/80, 10/90 or 0/100. In the second embodiment, representative proportions of non-absorbable material to absorbable material preferably comprise 100/0, 90/10, 80/20, 70/30 and 60/40. Medial layer **M'** can comprise the noted proportions of either of upper layer **U'** lower layer **L'**, or can comprise 50/50 absorbable/non-absorbable material. While representative proportions are provided herein, any suitable proportions can be employed in accordance with the present invention, and preferably, proportions are chosen depending on a particular end use for the scaffold of the present invention.

C. Method of Treating an Injury

A method of treating an injury in a subject is also provided in accordance with the present invention. The method comprises:

(a) providing a three-dimensional fiber scaffold formed of at least three systems of fibers, wherein two of the three fiber systems define an upper layer, a lower layer and a medial layer between the upper layer and the lower layer within the three-dimensional fiber scaffold, wherein one of the at least three fiber systems interconnects the upper layer, the lower layer and the medial layer, wherein the at least three systems of fibers each comprise a bio-compatible material; and

(b) placing the scaffold provided in step (a) at a site of injury in the subject to thereby repair the injury in the subject.

The subject treated in the present invention in its many embodiments is desirably a human subject, although it is to be understood that the principles of the invention indicate that the invention is effective with respect to all vertebrate species, including mammals, which are intended to be included in the term "subject". In this context, a mammal is understood to include any mammalian species in which treatment (i.e. repair) of an injury is desirable, particularly agricultural and domestic mammalian species.

The methods of the present invention are particularly useful in the treatment of warm-blooded vertebrates. Therefore, the invention concerns mammals and birds.

More particularly, contemplated is the treatment of mammals such as humans, as well as those mammals of importance due to being endangered (such as Siberian tigers), of economical importance (animals raised on farms for consumption by humans) and/or social importance (animals kept as pets or in zoos) to humans, for instance, carnivores other than humans (such as cats and dogs), swine (pigs, hogs, and wild boars), ruminants (such as cattle, oxen, sheep, giraffes, deer, goats, bison, and camels), and horses (e.g. race horses). Also contemplated is the treatment of birds, including the treatment of those kinds of birds that are endangered, kept in zoos (e.g. ostriches), as well as fowl, and more particularly domesticated fowl, i.e., poultry, such as turkeys, chickens, ducks, geese, guinea fowl, and the like, as they are also of economical importance to humans. Thus, contemplated is the treatment of

livestock, including, but not limited to, domesticated swine (pigs and hogs), ruminants, horses, poultry, and the like.

The scaffolds of the present invention are strong, yet flexible, thus reducing pain and discomfort for the subject. The scaffolds of the present invention can be used to treat small wounds, and in a preferred embodiment, are used to treat large wounds (e.g. ≥ 10 cm X 10 cm). The ability to customize porosity and free volume along with the unique cross-sections of fibers provided in accordance with the present invention facilitate cell proliferation and tissue ingrowth via channeling. These aid in angiogenesis, fibroplasia, and other mechanisms necessary for wound healing. Fast tissue incorporation also reduces or eliminates hematoma, seroma or fistula formation, as well as infection.

Absorbable meshes provided in the prior art have been shown to lose their strength before sufficient fibrous ingrowth occurs. Because of (a) the unique porous structures which induce fast and intimate tissue incorporation, and (b) exceptional strength properties, the use of a totally absorbable scaffold in injury repair is now provided by the scaffold of the present invention. Correspondingly, shrinkage of the present inventive scaffold is much less as compared to prior art structures. The controlled pore size and pore fraction of the present inventive scaffold coupled with the controlled geometry of the individual fibers and the controlled rate of bio-degradation also allow for site-specific delivery of chemicals at the wound or injury site to treat the wound or injury.

The thickness of the various layers, and thereby of the entire scaffold, can be altered and customized to fit many surgical indications. The scaffolds of the present invention thus constitute a new generation of lightweight, high-strength meshes for repairing hernia and traumatic injuries. Temporary use of a scaffold of the present invention is also feasible and entails a totally tightly woven or laminated/coated scaffold to prevent tissue ingrowth.

When employed, the methods and products of the present invention thus provide a variety of economic benefits, including reducing of medical costs, decreasing number of days of missed work, and prolonging life, among

other benefits.

The present co-inventors have developed a new three-dimensional fiber scaffold, wherein the three-dimensional fiber scaffold is formed with fiber systems comprising materials that have been selected to impart improved strength, flexibility and resorbability characteristics to the scaffold. Therefore, a new generation of scaffolds for injury and trauma repair along with methods of making and using the same have been provided in accordance with the present invention.

It will be understood that various details of the invention can be changed without departing from the scope of the invention. Furthermore, the foregoing description is for the purpose of illustration only, and not for the purpose of limitation--the invention being defined by the claims.

CLAIMS

What is claimed is:

1. A three-dimensional fiber scaffold for use in injury repair, the scaffold comprising at least three systems of fibers, wherein two of the three fiber systems define an upper layer, a lower layer and a medial layer between the upper layer and the lower layer within the three-dimensional fiber scaffold, wherein one of the at least three fiber systems interconnects the upper layer, the lower layer and the medial layer, and wherein the at least three fiber systems each comprise a bio-compatible material.

2. The three-dimensional fiber scaffold of claim 1, wherein the bio-compatible material comprises a material selected from the group consisting of an absorbable material, a non-absorbable material and combinations thereof.

3. The three-dimensional fiber scaffold of claim 2, wherein the non-absorbable material is selected from the group consisting of polypropylene, polyester, polytetrafluoroethylene (PTFE), expanded PTFE (ePTFE), polyethylene, polyurethane, polyamide, nylon, polyetheretherketone (PEEK), polysulfone, a cellulosic, fiberglass, an acrylic, tantalum, polyvinyl alcohol, carbon, ceramic, a metal, and combinations thereof.

4. The three-dimensional fiber scaffold of claim 2, wherein the absorbable material is selected from the group consisting of polyglycolic acid (PGA), polylactic acid (PLA), polyglycolide-lactide, polycaprolactone, polydioxanone, polyoxalate, a polyanhydride, a poly(phosphoester), catgut suture, collagen, silk, chitin, chitosan, hydroxyapatite, bioabsorbable calcium phosphate, hyaluronic acid, and combinations thereof.

5. The three-dimensional fiber scaffold of claim 2, wherein the fiber systems which define the upper layer comprise primarily an absorbable material, wherein the fiber systems which define the lower layer comprise primarily a non-absorbable material, and wherein the fiber systems which define the medial layer comprise both an absorbable material and a non-absorbable material.

6. The three-dimensional fiber scaffold of claim 1, wherein the fiber

systems further comprise a monofilament fiber, a multifilament fiber, a hollow fiber, a fiber having a variable cross-section along its length, or a combination thereof.

7. The three-dimensional fiber scaffold of claim 1, further comprising a plurality of contact points among the at least three fiber systems, and wherein two or more of the at least three fiber systems are secured to each other at one or more of the contact points.

8. The three-dimensional fiber scaffold of claim 1, wherein the at least three fiber systems in at least one of the upper, medial and lower layers define a plurality of interstices within the fiber scaffold.

9. The three-dimensional fiber scaffold of claim 8, wherein the interstices further comprise a pore size ranging from about 10 μm to about 250 μm.

10. The three-dimensional fiber scaffold of claim 9, wherein the interstices further comprise a pore size ranging from about 25 μm to about 175 μm.

11. The three-dimensional fiber scaffold of claim 10, wherein the interstices further comprise a pore size ranging from about 50 μm to about 125 μm.

12. The three-dimensional fiber scaffold of claim 8, wherein each of the upper, medial and lower layers have interstices, the medial layer comprising interstices that are smaller than the interstices present in the upper layer, and the lower layer comprising interstices that are smaller than the interstices present in the medial layer, to thereby facilitate cell contact guidance into the scaffold.

13. The three-dimensional fiber scaffold of claim 12, wherein the lower layer further comprises an outer surface, and the outer surface of the lower layer is free of interstices.

14. The three-dimensional fiber scaffold of claim 13, wherein the lower layer further comprises a cellular matrix.

15. The three-dimensional fiber scaffold of claim 1, wherein the lower layer of the three-dimensional fiber scaffold further comprises a coating.

16. The three-dimensional fiber scaffold of claim 15, wherein the coating comprises a resin.

17. The three-dimensional fiber scaffold of claim 16, wherein the resin further comprises a cellular matrix.

18. The three-dimensional fiber scaffold of claim 1, wherein at least one fiber in the fiber system that interconnects the upper, medial and lower layers further comprises a loop extending from the upper layer, to thereby facilitate tissue incorporation into the scaffold.

19. The three-dimensional fiber scaffold of claim 18, wherein the loop further comprises a pore size ranging from about 10 μm to about 250 μm.

20. The three-dimensional fiber scaffold of claim 19, wherein the loop further comprises a pore size ranging from about 25 μm to about 175 μm.

21. The three-dimensional fiber scaffold of claim 20, wherein the loop further comprises a pore size ranging from about 50 μm to about 125 μm.

22. The three-dimensional fiber scaffold of claim 1, wherein the three-dimensional fiber scaffold comprises three orthogonally woven fiber systems, a plurality of braided fiber systems, a plurality of circular woven fiber systems, or combinations thereof.

23. The three-dimensional fiber scaffold of claim 1, further comprising a therapeutic agent.

24. The three-dimensional fiber scaffold of claim 23, wherein the entire scaffold is impregnated with the therapeutic agent, wherein a layer of the scaffold is impregnated with the therapeutic agent, wherein an individual fiber within the scaffold is impregnated with a therapeutic agent, or wherein the scaffold comprises a hollow fiber and the therapeutic agent is loaded within an internal void space of the hollow fiber.

25. The three-dimensional fiber scaffold of claim 23, wherein the therapeutic agent comprises an anti-infective material.

26. The three-dimensional fiber scaffold of claim 25, wherein the anti-infective material is selected from the group consisting of povidone/iodine, silver, silver oxide, other silver salt, copper salts, sulfadiazine, chlorhexidine, triclosan, cetyl ammonium chloride, cetyl ammonium bromide, quaternary

amines, alkyl sulfonates and combinations thereof.

27. The three-dimensional fiber scaffold of claim 23, wherein the therapeutic agent comprises a cell growth modulating material.

28. The three-dimensional fiber scaffold of claim 27, wherein the cell growth modulating material is selected from the group consisting of a growth factor, a cytokine, a chemokine, a collagen, gelatin, laminin, fibronectin, thrombin, lipids, cartilage oligomeric protein (COMP), thrombospondin, fibrin, fibrinogen, Matrix-GLA (glycine-leucine-alanine) protein, chondrocalcin, tenascin, a mineral, an RGD (Arginine-Glycine-Aspartic Acid) peptide or RGD-peptide containing molecule, elastin, hyaluronic acid, a glycosaminoglycan, a proteoglycan, water, an electrolyte solution, and combinations thereof.

29. A method of producing a three-dimensional fiber scaffold for use in injury repair, the method comprising: forming a three-dimensional fiber scaffold with at least three fiber systems such that two of the three fiber systems define an upper layer, a lower layer and a medial layer between the upper layer and the lower layer within the three-dimensional fiber scaffold, and wherein one of the at least three fiber systems interconnects the upper layer, the lower layer and the medial layer, wherein the at least three fiber systems each comprise a bio-compatible material, whereby a three-dimensional fiber scaffold is produced.

30. The method of claim 29, wherein the bio-compatible material comprises a material selected from the group consisting of an absorbable material, a non-absorbable material and combinations thereof.

31. The method of claim 30, wherein the non-absorbable material is selected from the group consisting of polypropylene, polyester, polytetrafluoroethylene (PTFE), expanded PTFE (ePTFE), polyethylene, polyurethane, polyamide, nylon, polyetheretherketone (PEEK), polysulfone, a cellulosic, fiberglass, an acrylic, tantalum, polyvinyl alcohol, carbon, ceramic, a metal, and combinations thereof.

32. The method of claim 30, wherein the absorbable material is selected from the group consisting of polyglycolic acid (PGA), polylactic acid

(PLA), polyglycolide-lactide, polycaprolactone, polydioxanone, polyoxalate, a polyanhydride, a poly(phosphoester), catgut suture, collagen, silk, chitin, chitosan, hydroxyapatite, bioabsorbable calcium phosphate, hyaluronic acid, and combinations thereof.

33. The method of claim 30, wherein the fiber systems which define the upper layer comprise primarily an absorbable material, wherein the fiber systems which define the lower layer comprise primarily a non-absorbable material, and wherein the fiber systems which define the medial layer comprise both an absorbable material and a non-absorbable material.

34. The method of claim 29, wherein the fiber systems further comprise a monofilament fiber, a multifilament fiber, a hollow fiber, a fiber having a variable cross-section along its length, or a combination thereof.

35. The method of claim 29, further comprising forming a plurality of contact points within the three fiber systems and securing the at least three fiber systems to each other at the contact points.

36. The method of claim 29, further comprising forming the at least three fiber systems so that a plurality of interstices are defined in at least one of the upper, medial and lower layers within the fiber scaffold.

37. The method of claim 36, wherein the interstices further comprise a pore size ranging from about 10 μm to about 250 μm.

38. The method of claim 37, wherein the interstices further comprise a pore size ranging from about 25 μm to about 175 μm.

39. The method of claim 38, wherein the interstices further comprise a pore size ranging from about 50 μm to about 125 μm.

40. The method of claim 36, further comprising forming the at least three fiber systems so that a plurality of interstices are defined in each of the upper, medial and lower layers, the medial layer comprising interstices that are smaller than the interstices formed in the upper layer, and the lower layer comprising interstices that are smaller than the interstices formed in the medial layer, to thereby facilitate cell contact guidance into the scaffold.

41. The method of claim 40, further comprising forming an outer surface on the lower layer, wherein the outer surface of the lower layer is free

of interstices.

42. The method of claim 41, wherein the lower layer further comprises a cellular matrix.

43. The method of claim 29, wherein the lower layer of the three-dimensional fiber scaffold further comprises a coating.

44. The method of claim 43, wherein the coating comprises a resin.

45. The method of claim 44, wherein the resin further comprises a cellular matrix.

46. The method of claim 29, wherein at least one fiber in the fiber system that interconnects the upper, medial and lower layers further comprises a loop extending from the upper layer, to thereby facilitate tissue incorporation into the scaffold.

47. The method of claim 46, wherein the loop further comprises a pore size ranging from about 10 μm to about 250 μm.

48. The method of claim 47, wherein the loop further comprises a pore size ranging from about 25 μm to about 175 μm.

49. The method of claim 48, wherein the loop further comprises a pore size ranging from about 50 μm to about 125 μm.

50. The method of claim 29, wherein the three-dimensional fiber scaffold comprises three orthogonally woven fiber systems, a plurality of braided fiber systems, a plurality of circular woven fiber systems, or combinations thereof.

51. The method of claim 29, further comprising adding a therapeutic agent to the scaffold.

52. The method of claim 51, wherein the entire scaffold is impregnated with the therapeutic agent, wherein a layer of the scaffold is impregnated with the therapeutic agent, wherein an individual fiber within the scaffold is impregnated with a therapeutic agent, or wherein the scaffold comprises a hollow fiber and the therapeutic agent is loaded within an internal void space of the hollow fiber.

53. The method of claim 52, wherein the therapeutic agent comprises an anti-infective material.

54. The method of claim 53, wherein the anti-infective material is selected from the group consisting of povidone/iodine, silver, silver oxide, other silver salt, copper salts, sulfadiazine, chlorhexidine, triclosan, cetyl ammonium chloride, cetyl ammonium bromide, quaternary amines, alkyl sulfonates and combinations thereof.

55. The method of claim 51, wherein the therapeutic agent comprises a cell growth modulating material.

56. The method of claim 55, wherein the cell growth modulating material is selected from the group consisting of a growth factor, a cytokine, a chemokine, a collagen, gelatin, laminin, fibronectin, thrombin, lipids, cartilage oligomeric protein (COMP), thrombospondin, fibrin, fibrinogen, Matrix-GLA (glycine-leucine-alanine) protein, chondrocalcin, tenascin, a mineral, an RGD (Arginine-Glycine-Aspartic Acid) peptide or RGD-peptide containing molecule, elastin, hyaluronic acid, a glycosaminoglycan, a proteoglycan, water, an electrolyte solution, and combinations thereof.

57. A method of treating an injury in a subject, the method comprising:

(a) providing a three-dimensional fiber scaffold formed of at least three systems of fibers, wherein two of the three fiber systems define an upper layer, a lower layer and a medial layer between the upper layer and the lower layer within the three-dimensional fiber scaffold, wherein one of the at least three fiber systems interconnects the upper layer, the lower layer and the medial layer, wherein the at least three fiber systems each comprise a bio-compatible material; and

(b) placing in the subject at a site of an injury in the subject the three-dimensional fiber scaffold provided in step (a) to thereby repair an injury in the subject.

58. The method of claim 57, wherein the bio-compatible material comprises a material selected from the group consisting of an absorbable material, a non-absorbable material and combinations thereof.

59. The method of claim 58, wherein the non-absorbable material is

selected from the group consisting of polypropylene, polyester, polytetrafluoroethylene (PTFE), expanded PTFE (ePTFE), polyethylene, polyurethane, polyamide, nylon, polyetheretherketone (PEEK), polysulfone, a cellulosic, fiberglass, an acrylic, tantalum, polyvinyl alcohol, carbon, ceramic, a metal, and combinations thereof.

60. The method of claim 58, wherein the absorbable material is selected from the group consisting of polyglycolic acid (PGA), polylactic acid (PLA), polyglycolide-lactide, polycaprolactone, polydioxanone, polyoxalate, a polyanhydride, a poly(phosphoester), catgut suture, collagen, silk, chitin, chitosan, hydroxyapatite, bioabsorbable calcium phosphate, hyaluronic acid, and combinations thereof.

61. The method of claim 58, wherein the fiber systems which define the upper layer comprise primarily an absorbable material, wherein the fiber systems which define the lower layer comprise primarily a non-absorbable material, and wherein the fiber systems which define the medial layer comprise both an absorbable material and a non-absorbable material.

62. The method of claim 57, wherein the fiber systems further comprise a monofilament fiber, a multifilament fiber, a hollow fiber, a fiber having a variable cross-section along its length, or a combination thereof.

63. The method of claim 57, wherein the three-dimensional fiber scaffold further comprises a plurality of contact points among the at least three fiber systems, and wherein the at least three fiber systems are secured to each other at one or more of the contact points.

64. The method of claim 57, wherein the at least three fiber systems in at least one of the upper, medial and lower layers in the three-dimensional fiber scaffold define a plurality of interstices within the fiber scaffold.

65. The method of claim 64, wherein the interstices further comprise a pore size ranging from 10 µm to 250 µm.

66. The method of claim 65, wherein the interstices further comprise a pore size ranging from about 25 to about 175 µm.

67. The method of claim 66, wherein the interstices further comprise a pore size ranging from about 50 to about 125 µm.

68. The method of claim 64, wherein each of the upper, medial and lower layers have interstices, the medial layer comprising interstices that are smaller than the interstices present in the upper layer, and the lower layer comprising interstices that are smaller than the interstices present in the medial layer, to thereby facilitate cell contact guidance into the scaffold.

69. The method of claim 68, further comprising forming an outer surface on the lower layer, wherein the outer surface of the lower layer is free of interstices.

70. The method of claim 69, wherein the lower layer further comprises a cellular matrix.

71. The method of claim 57, wherein the lower layer of the three-dimensional fiber scaffold further comprises a coating.

72. The method of claim 71, wherein the coating comprises a resin.

73. The method of claim 72, wherein the resin further comprises a cellular matrix.

74. The method of claim 57, wherein at least one fiber in the fiber system that interconnects the upper, medial and lower layers further comprises a loop extending from the upper layer, to thereby facilitate tissue incorporation into the scaffold.

75. The method of claim 74, wherein the loop further comprises a pore size ranging from about 10 μm to about 250 μm.

76. The method of claim 75, wherein the loop further comprises a pore size ranging from about 25 μm to about 175 μm.

77. The method of claim 76, wherein the loop further comprises a pore size ranging from about 50 μm to about 125 μm.

78. The method of claim 57, wherein the three-dimensional fiber scaffold comprises three orthogonally woven fiber systems, a plurality of braided fiber systems, a plurality of circular woven fiber systems, or combinations thereof.

79. The method of claim 57, wherein the scaffold further comprises a therapeutic agent.

80. The method of claim 79, wherein the entire scaffold is

impregnated with the therapeutic agent, wherein a layer of the scaffold is impregnated with the therapeutic agent, wherein an individual fiber within the scaffold is impregnated with a therapeutic agent, or wherein the scaffold comprises a hollow fiber and the therapeutic agent is loaded within an internal void space of the hollow fiber.

81. The method of claim 79, wherein the therapeutic agent comprises an anti-infective material.

82. The method of claim 81, wherein the anti-infective material is selected from the group consisting of povidone/iodine, silver, silver oxide, other silver salt, copper salts, sulfadiazine, chlorhexidine, triclosan, cetyl ammonium chloride, cetyl ammonium bromide, quaternary amines, alkyl sulfonates and combinations thereof.

83. The method of claim 79, wherein the therapeutic agent comprises a cell growth modulating material.

84. The method of claim 83, wherein the cell growth modulating material is selected from the group consisting of a growth factor, a cytokine, a chemokine, a collagen, gelatin, laminin, fibronectin, thrombin, lipids, cartilage oligomeric protein (COMP), thrombospondin, fibrin, fibrinogen, Matrix-GLA (glycine-leucine-alanine) protein, chondrocalcin, tenascin, a mineral, an RGD (Arginine-Glycine-Aspartic Acid) peptide or RGD-peptide containing molecule, elastin, hyaluronic acid, a glycosaminoglycan, a proteoglycan, water, an electrolyte solution, and combinations thereof.

85. The method of claim 57, wherein the injury is an internal injury.

86. The method of claim 85, wherein the scaffold is placed in the injury so that a lower layer of the scaffold is adjacent to a peritoneal cavity in the subject.

87. The method of claim 86, wherein each of the upper, medial and lower layers have interstices, the medial layer comprising interstices that are smaller than the interstices present in the upper layer, and the lower layer comprising interstices that are smaller than the interstices present in the medial layer, to thereby facilitate cell contact guidance into the scaffold via the upper layer and to thereby inhibit cell ingrowth into the lower layer.

FIG. 1

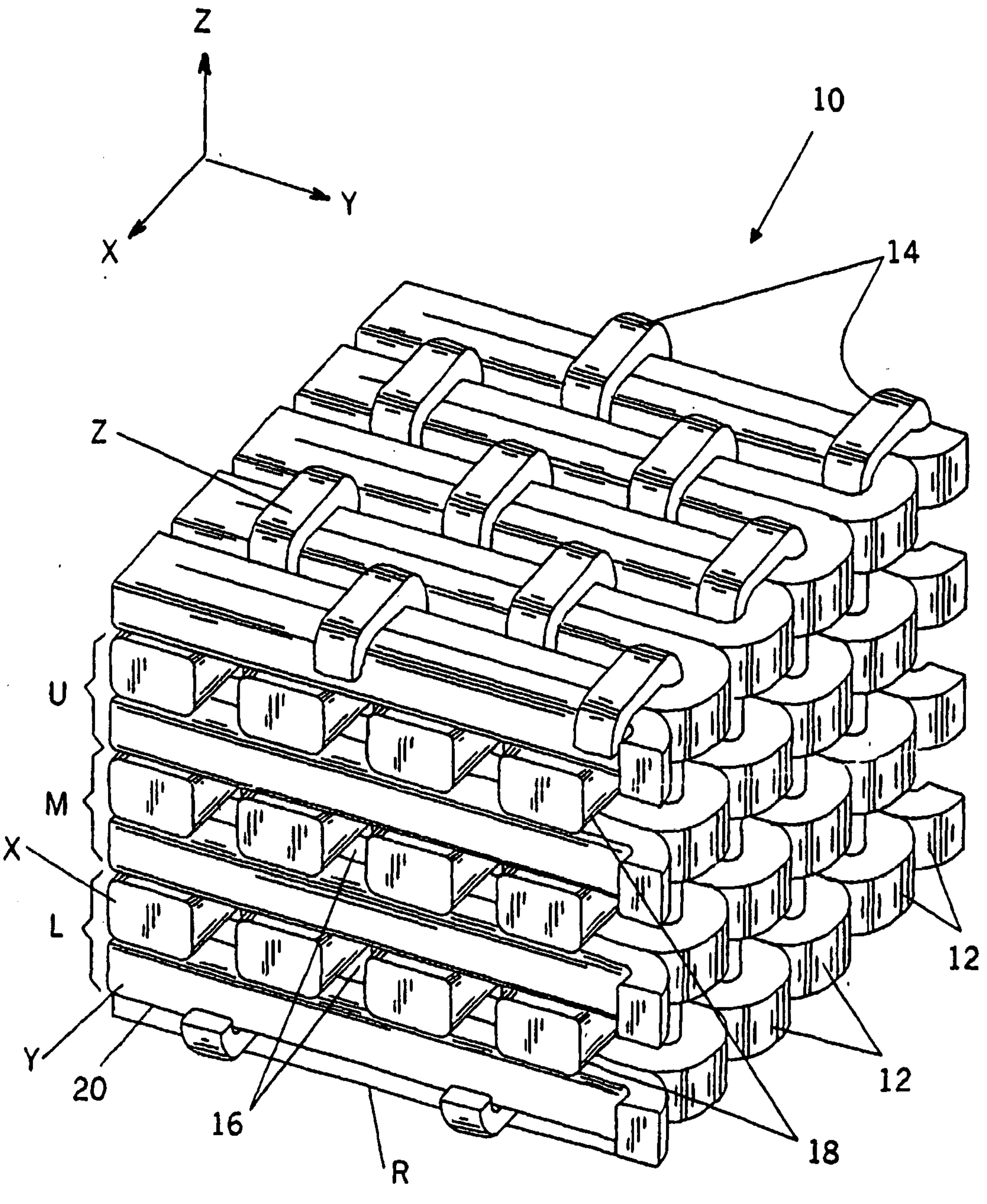


FIG. 2

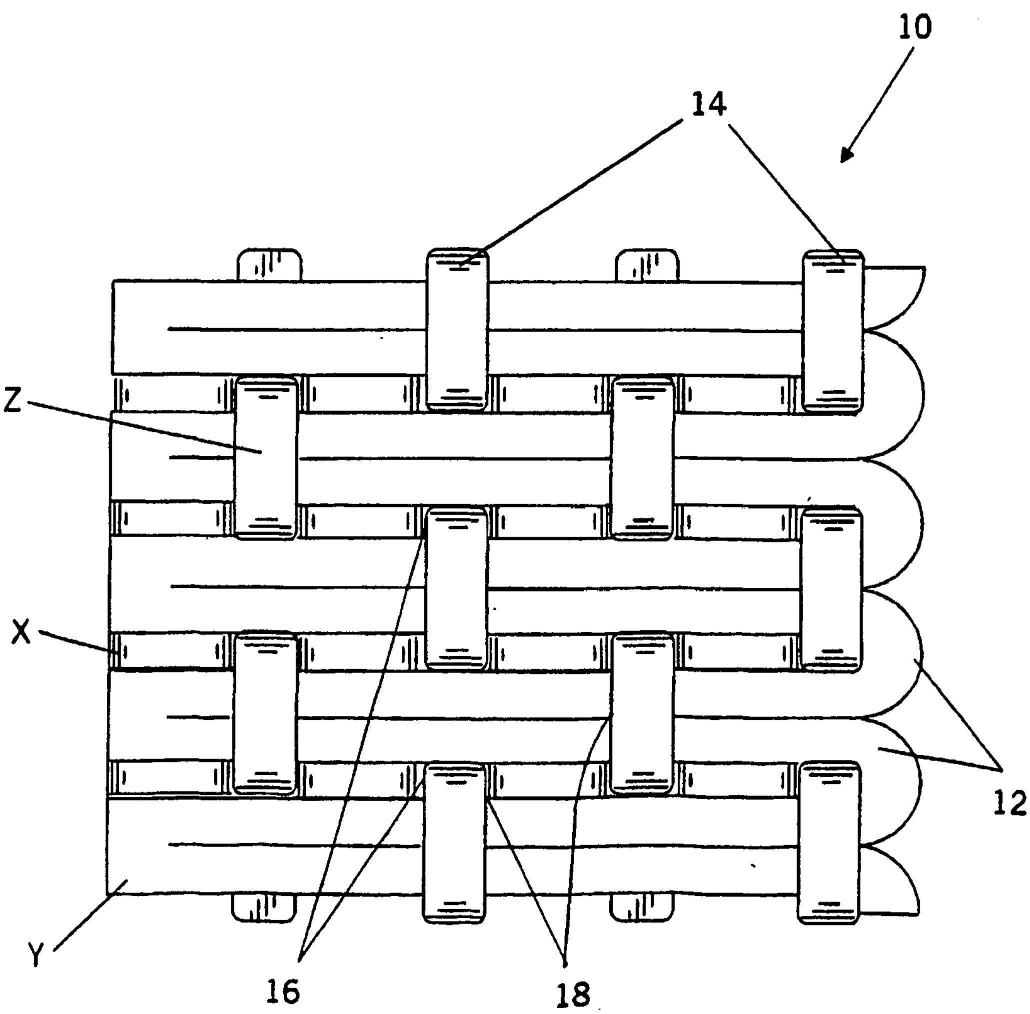
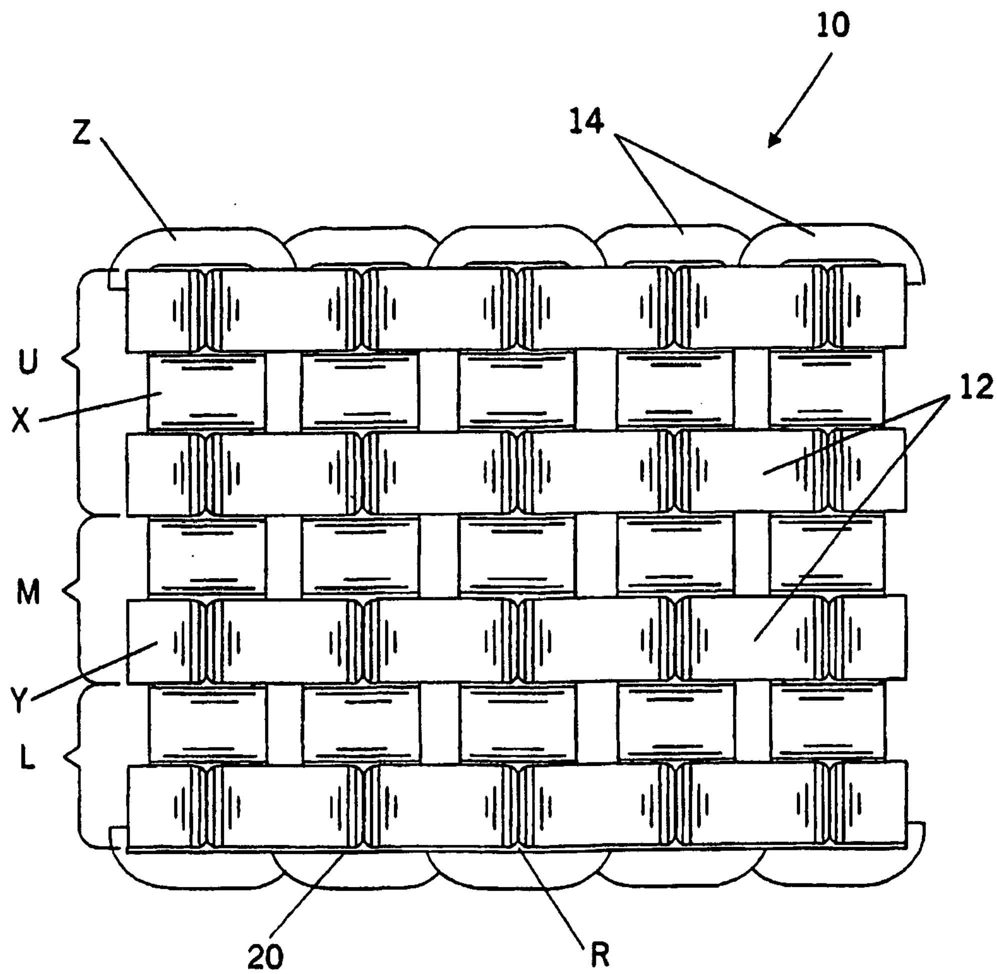


FIG. 3



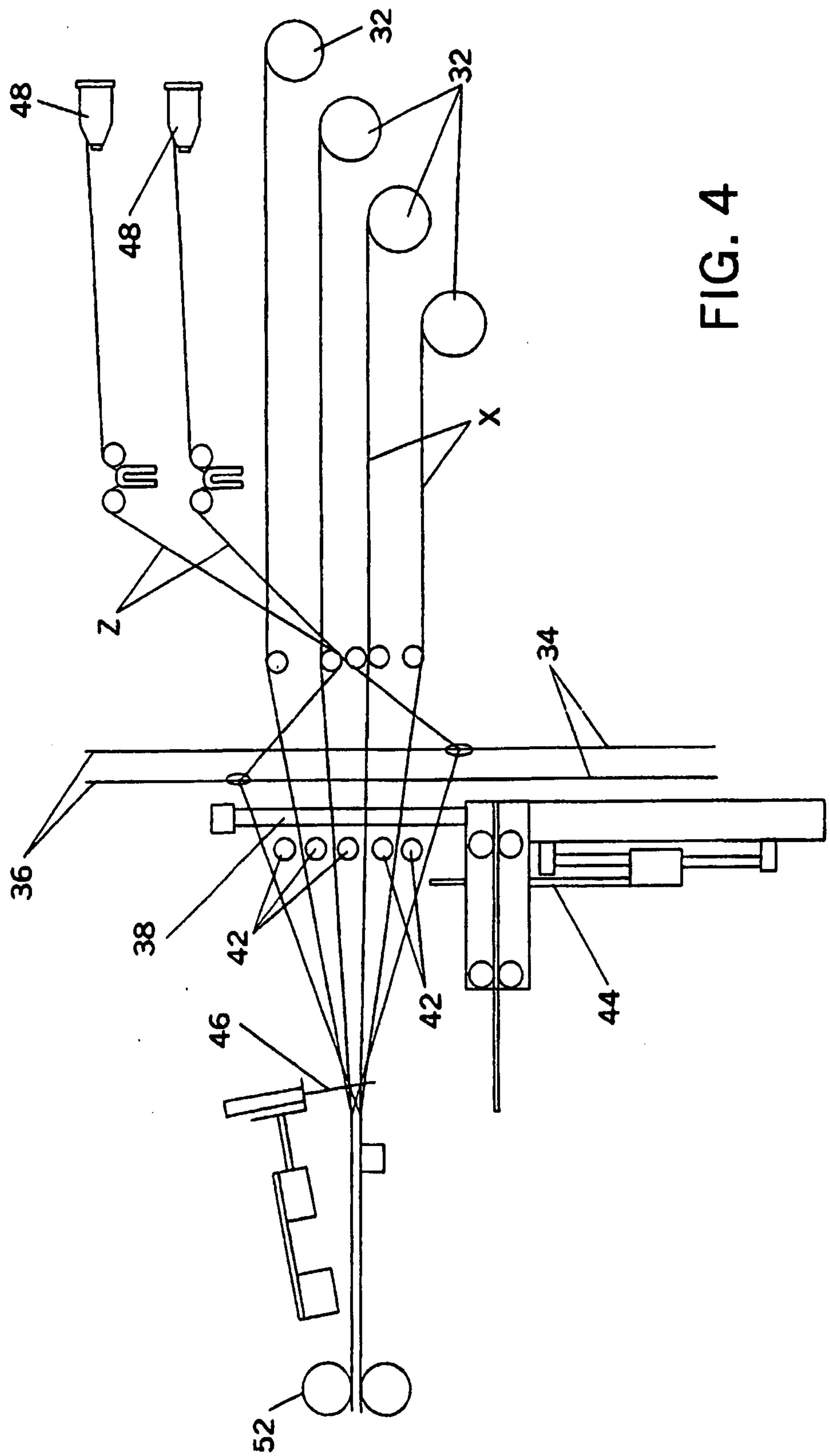


FIG. 4

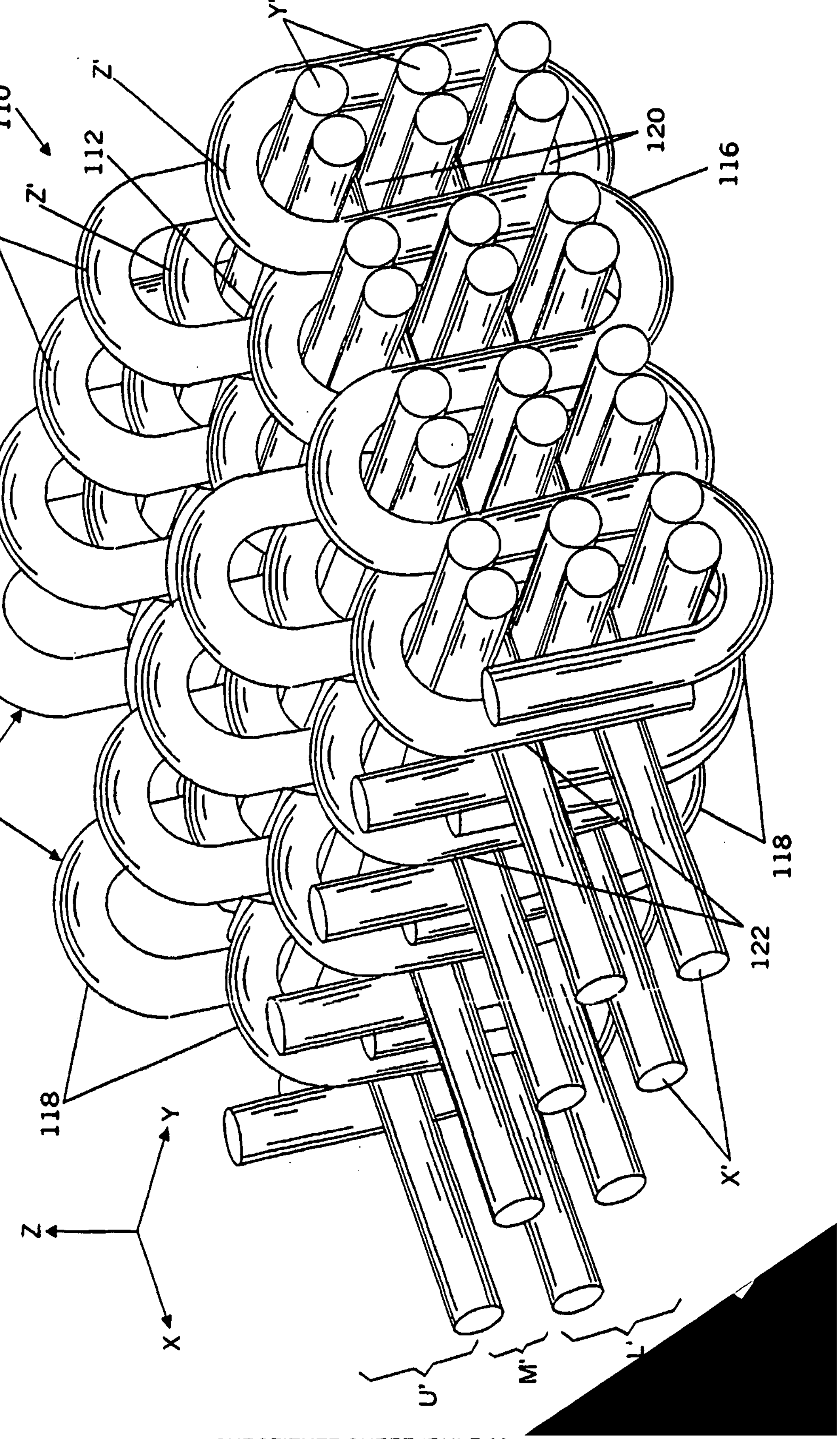


FIG. 5

FIG. 6